II. REMARKS

Formal Matters

Claims 1, 3, 4, 6-17, and 24-27 are pending after entry of the amendments set forth herein.

Claims 1-9, 12-14, 16, 17, and 24-26 were examined. Claims 1, 2, 6-9, 12, 13, and 24-26 were rejected. Claims 3-5, 14, 16, and 17 were allowed. Claims 10, 11, 15, and 18-23 were withdrawn from consideration.

Claims 1, 3, 6-9, 24 and 25 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. The amendments to claim 6 find support in the specification at, e.g., paragraphs 0086 and 0087. No new matter is added by the amendments to claims 1, 3, 6-9, 24, and 25.

Claims 2, 5, and 18-23 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

New claim 27 is added. No new matter is introduced by new claim 27.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Withdrawn rejections

Applicants note with gratitude that the following objections and rejections, raised in the Office Action mailed November 28, 2006, were withdrawn: 1) objection to claim 7; 2) objection to claims 2 and 5-9; 3) rejection of claims 3-5 under 35 U.S.C. §102(e); 4) rejection of claims 1, 2, and 12 under 35 U.S.C. §102(b); and 5) rejection of claims 3, 4, 14, 16, and 17 under 35 U.S.C. §103(a).

Allowed claims

Page 1 of the Office Action indicated that claims 3-5, 14, 16, and 17 were allowed. However, page 4 of the Office Action indicates that claims 3-5, 14, 16, and 17 are rejected. Applicants request clarification of the status of claims 3-5, 14, 16, and 17.

Double patenting

Claims 1-2, 6-9, 12, 13, and 24-26 were rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1-9 and 15 of U.S. Patent No. 6,498,148.

Upon an indication of allowance of the instant claims, Applicants will consider filing a Terminal Disclaimer.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-17 and 24-26 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

The Office Action stated that the specification is enabling for "some sequences" containing CpG. The Office Action stated that the specification does not reasonably provide enablement for all TLR agonists.

Claims 1 and 3 are amended to recite administration of a TLR9 agonist, wherein the TLR9 agonist is a nucleic acid comprising the sequence 5'-CG-3'.

The Office Action reviewed some of the Wands factors.[1]

Guidance in the specification

The instant specification provides ample guidance for TLR9 agonists that are nucleic acids comprising the sequence 5'-CG-3'. Specification, paragraphs 0083-0093. Numerous examples of CG-containing motifs that are suitable for use in a subject method are provided. The claims recite that the nucleic acids are TLR9 agonists. Thus, any CG-containing nucleic acid that is not a TLR9 agonist is specifically excluded from the scope of the claims.

The Office Action stated that "[n]o guidance is provided in determining which CpG sequences should be used for the successful practice of the claimed methods." Office Action, page 5. However, the specification states that a "therapeutic CpG-containing nucleic acid suitable for use in a subject method can be readily identified, e.g., by using an animal model of chronic asthma as described in the Examples, or using a bleomycin-induced animal model of lung fibrosis." Thus, the specification provides at least two different ways, **including working examples**, to determine whether a given CG-containing nucleic acid will be efficacious.

Predictability of the art.

The office Action stated that the physiological art in general is acknowledged to be unpredictable. While there may be some non-functional variants within the genus defined by nucleic acids comprising the sequence 5'-CG-3', the courts have clearly taught that even in unpredictable arts the specification does not have to disclose every species of a genus that would work and every species that would not work.

The Office Action stated that Applicant has not provided any common structure (e.g., motifs) that would lead to the function as claimed. However, as noted above, the instant specification provides ample guidance for TLR9 agonists that are nucleic acids comprising the sequence 5'-CG-3'. Specification, paragraphs 0083-0093. Numerous examples of CG-containing motifs that are suitable for use in a subject method are provided. Such motifs include, e.g., 5'-purine-purine-CG-pyrimidine-pyrimidine-3', 5'-purine-TCG-pyrimidine-pyrimidine-3'; $(TCG)_n$, where $n \geq 1$, and the like. See, e.g., paragraph 0086.

[1] *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988)

Working examples

The Office Action stated that the examples do not show that all CpG sequences can be used to treat chronic asthma, wherein airway remodeling is reduced.

However, Applicants are not required to provide working examples showing that every embodiment will work. While there may be some non-functional CG-containing nucleic acids within the genus "nucleic acid comprising 5'-CG-3'," the courts have clearly taught that even in unpredictable arts the specification does not have to disclose every species of a genus that would work and every species that would not work.

The court has very clearly explained[2]:

> "To require such a complete disclosure would apparently necessitate a patent application or applications with thousands of catalysts….More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid literal infringement of such claims by merely finding another analogous catalyst complex which could be used …."

Applicants provided working examples showing that a TLR9 agonist having the sequence 5'-TGACTGTGAACGTTCGAGATGA-3'. This TLR9 agonist includes the motif 5'-purine-purine-CG-pyrimidine-pyrimidine-3' (see underlined motif: 5'-TGACTGTGAACGTTCGAGATGA-3') as well as the motif 5'-$(TCG)_n$, where n is ≥ 1.

Amount of experimentation necessary

The Office Action stated that it would require "much experimentation" to ascertain both the structure and function of the CpG sequences that would lead to successful practice of the claimed methods. Office Action, page 5.

The courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP §2164.01.[3]

As the court explained[4]:

> "[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."

Practitioners in the chemical and molecular biology arts frequently engage in extensive modification of

[2] *In re Angstadt*, 190 USPQ 214, at 219 (CCPA 1976)
[3] See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue in the molecular biology arts. For example, the court concluded that extensive screening experiments, while being voluminous, were not undue in view of the art which routinely performs such long experiments.[5]

The claimed methods recite administration of a TLR9 agonist, where the TLR9 agonist is a nucleic acid comprising the sequence 5'-CG-3'. The only experiments, if any, that need be performed to enable the entire scope of the claim are those designed to determine which CG-containing nucleic acids retain the ability to reduce airway remodeling or reduce interstitial lung fibrosis. Such nucleic acids are determined through routine experimentation, typically employing nothing more than performing the same assay disclosed in the specification on a variety of nucleic acids, e.g., nucleic acids comprising a CG-containing sequence motif disclosed in the specification. Since these experiments are routine in nature, no undue experimentation is required. In other words, the only experimentation that may be required to enable the claimed invention are those experiments to determine the presence of a certain activity, and since this only requires a routine assay on various nucleic acids to determine the active variants, no undue experimentation is necessary.

Conclusion as to the rejection under 35 U.S.C. §112, first paragraph

Applicants submit that the rejection of claims 1-17 and 24-26 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

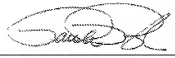
[4] *In re Wands* 8 USPQ 2d at 1404
[5] *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSD-292.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: January 16, 2008 By: 

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